REMARKS

Entry of the foregoing, reexamination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested.

By the foregoing amendment, claims 33 and 36 have been amended to further clarify Applicant's invention. Support for the amendments can be found throughout the specification. Further new claims 41-43 have been added. Support for new claims 41-43 can be found in original claim 1 (claim 41) and on pages 14 and 15 (paragraph bridging pages 14 and 15) of the specification (claims 42-43). Accordingly no new matter has been added.

I. Rejections under 35 U.S.C. § 112, second paragraph

Claim 40 has been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for not setting forth any steps involved in the process or method. This rejection is rendered moot in light of the cancellation of claim 40. However, to the extent that this rejection may apply to new claim 41, it is respectfully traversed.

Claim 41, which replaces claim 40, recites specific steps of contacting, cleaving and sequence determination. Therefore, Applicants respectfully request withdrawal of the rejection of claim 40 under 35 U.S.C. § 112, second paragraph.

II. Rejections under 35 U.S.C. § 101

Claim 40 has also been rejected under 35 U.S.C. § 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper

definition of a process. This rejection is rendered moot in light of the cancellation of claim 40. However, to the extent that this rejection may apply to claim 41, it is respectfully traversed.

As stated above, claim 41, which replaces claim 40, recites specific steps of contacting, cleaving and sequence determination. Therefore, Applicants respectfully request withdrawal of the rejection of claim 40 under 35 U.S.C. § 101.

III. Rejections under 35 U.S.C. § 102(b)

Claims 21-32 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Southern et al. (WO 95/04160). Applicants respectfully traverse this rejection.

It is well settled law that to anticipate a claim, a single reference must teach each and every element of the claim, and the single reference must be enabling. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802F.2d 1367, 1379, 231 U.S.P.Q. 81, 90 (Fed. Cir. 1986); *Atlas Powder Co. v. E.I du Pont De Nemours & Co.*, 750 F.2d 1569, 1574, 224 U.S.P.Q. 409, 411 (Fed. Cir. 1984).

Applicants submit that the presently-claimed invention is directed to a method for sequencing multiple DNA templates in the same reaction zone. By contrast, the method disclosed in Southern et al., in particular pages 14 to 21 of Southern et al., is suitable only for sequencing a single DNA template. Southern et al. does disclose the sequencing of multiple templates in parallel, however, each of these templates is present in its own distinct reaction zone (*e.g.*, on a pin) and sequencing involves simply carrying out the disclosed method of each template separately.

This type of parallel analysis of multiple templates represents a fundamentally different problem from the analysis of multiple templates in the same reaction zone, as described in the present invention. In particular, if multiple templates are to be analyzed in a single reaction zone, there must be some method of analyzing the data from the reaction zone so that particular data can be assigned to the particular template that generated it.

For this reason, the presently-claimed invention requires that each DNA template is present in the reaction zone in a unique amount. In any given sequencing cycle, the frequency of (or signal size from) each probe will vary with the amount of the complementary DNA template present in the reaction zone.

By comparison, Southern et al. is not concerned with the problem of analyzing multiple templates in the same reaction zone, and thus, the method of Southern et al. would not be suitable for that purpose.

Because Southern et al. does not teach each and every element of the claim, as required by law, the reference can not anticipate the claimed invention. Therefore, Applicants respectfully request the withdrawal of the rejection of claims 21-32 under 35 U.S.C. § 102(b).

Claims 21-25 and 27-32 have been rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Macevicz et al. (WO 96/33205). Applicants respectfully traverse this rejection.

Applicants submit that the presently-claimed invention is distinct from the disclosure in Macevicz et al., on the basis that Macevicz et al. does not disclose a method for sequencing multiple different templates in the same reaction zone.

Macevicz et al. instead provides a method for analyzing a single nucleic acid template by dividing a population comprising multiple copies of that template into several reaction zones. In each reaction zone, a different initializing oligonucleotide is added to the target template so that each initializing oligonucleotide starts sequencing at a different point in the target sequence. For example, each oligonucleotide may start the sequencing reaction one base further along the target. Probe oligonucleotides are then ligated to the initializing oligonucleotide, identifying the base adjacent to the initializing oligonucleotide. In this way, several bases of the sequence are identified for each target, but at the expense of having multiple parallel reaction zones for each template.

The method of Macevicz et al. is therefore entirely different from the presently-claimed method in which multiple different templates are sequenced simultaneously in the same reaction zone.

It appears that the Examiner does not seem to have made a distinction between (a) a target population which comprises more than one copy of the single nucleic acid template in a single reaction zone; and (b) a target population in which there are several different nucleic acid templates, each template being present in multiple copies in the reaction zone, and each template being present in a unique amount with respect to the other templates in the reaction zone.

Furthermore, it would not be possible for the skilled artisan to arrive at the presently-claimed method by combining the teaching of Southern et al. and Macevicz et al. since Macevicz et al. also does not address the problem of sequencing multiple different templates in one reaction zone.

Southern et al. and Macevicz et al. are concerned only with the type (a) target population while the presently-claimed method is concerned with the type (b) target population.

Because Macevicz et al. does not teach each and every element of the claim, as required by law, the reference can not anticipate the claimed invention. Therefore, Applicants respectfully request the withdrawal of the rejection of claims 21-25 and 27-32 under 35 U.S.C. § 102(a).

IV. Rejections under 35 U.S.C. § 103(a)

Claims 21-39 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Southern et al. in view of Stratagene Catalog (page 39, 1988). Applicants respectfully traverse this rejection.

Applicants submit that as noted above, Southern et al. does not address the problem of sequencing multiple different templates in the same reaction zone. The method disclosed in Southern et al. would not be suitable for this purpose, and there is no teaching or suggestion in the document of how the method might be adapted to make it suitable. Indeed, since Southern et al. is silent with regard to sequencing different multiple templates in one reaction zone. Upon reading Southern et al. the skilled artisan would not be motivated to attempt to

adapt the teaching of Southern et al. to arrive at a method falling within the scope of present invention.

The Examiner appears to find that the claims lack an inventive step, on the basis that a person skilled in the art would be motivated by the contents of the Stratagene Catalogue (1988 page 39) to modify the teaching of Southern et al. by combining the reagents for DNA sequencing into a kit.

As discussed above, the presently-claimed invention provides a method for sequencing multiple different templates in the same reaction zone. The method requires that each template is present in the reaction zone in a unique amount. In any given sequencing cycle, a probe can be linked with a particular template or templates on the basis that the signal size from each probe will vary with the amount of the complementary DNA template present in the reaction zone.

In order for the presently-claimed method to work, the data obtained - the frequency of (or signal size from) each probe for each sequencing cycle - must be further resolved into the various template sequences. There is a possibility that two template sequences will have the same subsequence in the sequencing cycle, so that the frequency of (or signal size from) the probe complementary to that subsequence will correspond to the sum of those template frequencies. The method for analyzing the data must be able to resolve these ambiguities.

On page 14 of the present application, it is noted that the present invention includes an algorithm for analyzing the data obtained in the presently-claimed sequencing method. The algorithm resolves the frequency of (or signal size from) each hybridized probe into quantities which relate to the unique amount of each template.

In view of the above, claim 33 of the present application has been amended firstly to include the feature that the kit is for sequencing a plurality of DNA templates, each present in a unique amount in the same reaction zone. Secondly, claim 33 has been amended to include a means for resolving the data obtained in the sequencing reaction. Support for these features may be found on pages 6 to 7 and pages 14 to 15 of the present application, respectively.

New claims 41 and 42 further define the means in claim 33 (part (b) of claim 33) as an algorithm or a computer program. Again, support for these new claims may be found on page 14 of the application.

Neither Southern et al. nor Macevicz et al. discloses the sequencing kit of claim 33. In particular, neither document discloses a means for resolving hybridization data obtained from a plurality of DNA templates from the same reaction zone, based on the unique amount in which each of the templates is present in the reaction zone.

Furthermore, neither Southern et al. nor Macevicz et al. in any way suggests the kit of present claim 33. It would not be possible for a skilled person to combine the teaching of Southern et al. and Macevicz et al. or the teaching of Southern et al. and Macevicz et al. with the contents of the cited Stratagene Catalogue in order to arrive at a kit falling within the scope of present claim 33.

Based on the foregoing, this application is believed to be in condition for allowance. A Notice to that effect is respectfully solicited. However, if any issues remain outstanding after consideration of this Reply, the Examiner is respectfully requested to contact the undersigned so that prosecution may be expedited.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: _____
Teresa Stanek Rea
Registration No. 30,427

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620

Date: October 12, 2000